Aicardi syndrome

Aicardi syndrome is a disorder that occurs almost exclusively in females. It is characterized by three main features that occur together in most affected individuals. People with Aicardi syndrome have absent or underdeveloped tissue connecting the left and right halves of the brain (agenesis or dysgenesis of the corpus callosum). They have seizures beginning in infancy (infantile spasms), which tend to progress to recurrent seizures (epilepsy) that can be difficult to treat. Affected individuals also have chorioretinal lacunae, which are defects in the light-sensitive tissue at the back of the eye (retina).

People with Aicardi syndrome often have additional brain abnormalities, including asymmetry between the two sides of the brain, brain folds and grooves that are small in size or reduced in number, cysts, and enlargement of the fluid-filled cavities (ventricles) near the center of the brain. Some have an unusually small head (microcephaly). Most affected individuals have moderate to severe developmental delay and intellectual disability, although some people with this disorder have milder disability.

In addition to chorioretinal lacunae, people with Aicardi syndrome may have other eye abnormalities such as small or poorly developed eyes (microphthalmia) or a gap or hole (coloboma) in the optic nerve, a structure that carries information from the eye to the brain. These eye abnormalities may cause blindness in affected individuals.

Some people with Aicardi syndrome have unusual facial features including a short area between the upper lip and the nose (philtrum), a flat nose with an upturned tip, large ears, and sparse eyebrows. Other features of this condition include small hands, hand malformations, and spinal and rib abnormalities leading to progressive abnormal curvature of the spine (scoliosis). They often have gastrointestinal problems such as constipation or diarrhea, gastroesophageal reflux, and difficulty feeding.

The severity of Aicardi syndrome varies. Some people with this disorder have very severe epilepsy and may not survive past childhood. Less severely affected individuals may live into adulthood with milder signs and symptoms.

Frequency

Aicardi syndrome is a very rare disorder. It occurs in about 1 in 105,000 to 167,000 newborns in the United States. Researchers estimate that there are approximately 4,000 affected individuals worldwide.

Genetic Changes

The cause of Aicardi syndrome is unknown. Because it occurs almost exclusively in females, researchers believe that it is probably the result of a mutation in a gene on the X chromosome. People normally have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Genes on these chromosomes are also involved in other functions in the body. Females typically have two X chromosomes (46,XX), and males have one X chromosome and one Y chromosome (46,XY).

Early in embryonic development in females, one of the two X chromosomes is permanently inactivated in somatic cells (cells other than egg and sperm cells). X-inactivation ensures that females, like males, have only one active copy of the X chromosome in each body cell. Usually X-inactivation occurs randomly, so that each X chromosome is active in about half the body's cells. Sometimes X-inactivation is not random, and one X chromosome is active in more than half of cells. When X-inactivation does not occur randomly, it is called skewed X-inactivation.

Skewed X-inactivation sometimes occurs when there is a severe gene mutation in one of the X chromosomes in each cell. Because the cells where this chromosome is active will not be able to survive as well, X-inactivation will appear to be skewed. Skewed X-inactivation has been identified in girls with Aicardi syndrome, further supporting the idea that the disorder is caused by a mutation in a gene on the X chromosome. However, this gene has not been identified, and it is unknown how the genetic change that causes Aicardi syndrome results in the various signs and symptoms of this disorder.

Inheritance Pattern

Nearly all known cases of Aicardi syndrome are sporadic, which means that they are not passed down through generations and occur in people with no history of the disorder in their family. The disorder is believed to result from new gene mutations.

Aicardi syndrome is classified as an X-linked dominant condition. While the gene associated with this disorder is not known, it is believed to be located on the X chromosome. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell is nearly always lethal very early in development, so almost all babies with Aicardi syndrome are female. However, a few affected males with an extra copy of the X chromosome in each cell (47,XXY) have been identified. Males with a 47,XXY chromosome pattern also have a condition called Klinefelter syndrome.

Other Names for This Condition

- agenesis of corpus callosum with chorioretinal abnormality
- agenesis of corpus callosum with infantile spasms and ocular abnormalities
- Aicardi's syndrome
- callosal agenesis and ocular abnormalities
- chorioretinal anomalies with ACC

Diagnosis & Management

These resources address the diagnosis or management of Aicardi syndrome:

- Baylor College of Medicine
  https://www.bcm.edu/research/labs/ignatia-van-den-veyver/research-areas/aicardi-syndrome
- GeneReview: Aicardi Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1381
- Genetic Testing Registry: Aicardi's syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0175713/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Aicardi Syndrome
  https://medlineplus.gov/ency/article/001664.htm
- Health Topic: Brain Malformations
  https://medlineplus.gov/brainmalformations.html
- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html

Genetic and Rare Diseases Information Center

- Corpus callosum agenesis
  https://rarediseases.info.nih.gov/diseases/1535/corpus-callosum-agenesis

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke (NINDS): Agenesis of the Corpus Callosum
  https://www.ninds.nih.gov/Disorders/All-Disorders/Agenesis-Corpus-Callosum-Information-Page
- National Institute of Neurological Disorders and Stroke (NINDS): Aicardi Syndrome
  https://www.ninds.nih.gov/Disorders/All-Disorders/Aicardi-Syndrome-Information-Page

Educational Resources

- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Disease InfoSearch: Aicardi Syndrome
  http://www.diseaseinfosearch.org/Aicardi+Syndrome/274
- MalaCards: aicardi syndrome
  http://www.malacards.org/card/aicardi_syndrome
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Aicardi%20syndrome&type=profile
- National Association of Special Education Teachers
  http://www.naset.org/aicardi1.0.html
- Orphanet: Aicardi syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=50

Patient Support and Advocacy Resources

- National Organization for Disorders of the Corpus Callosum
  http://nodcc.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/aicardi-syndrome/
- University of Kansas: Support Groups for Aicardi Syndrome
  http://www.kumc.edu/gec/support/aicardi.html

GeneReviews

- Aicardi Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1381

Genetic Testing Registry

- Aicardi's syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0175713/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Aicardi+syndrome%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28aicardi+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- AICARDI SYNDROME
  http://omim.org/entry/304050

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